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Oral presentation

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Background

Evidence suggests that CD8 T cells are important to the control of HIV replication in elite controllers. However, the mechanism behind the enhanced suppressive capacity of CD8 T cells in these subjects remains unclear.

Methods

We have recently discovered the novel ability of human CD8 T cells to rapidly upregulate perforin following antigen-specific stimulation. Using polychromatic flow cytometry and standard intracellular cytokine staining assays, we measured perforin expression, cytokine production, and degranulation by CD8 T cells following stimulation using overlapping peptide pools encompassing the entire HIV proteome. We studied several HIV-infected groups that differentially control viral replication off therapy: elite controllers (n = 34), viremic controllers (n = 29), chronic progressors (n = 24), and viremic nonprogressors (n = 6).

Results

We observe that on average 40% of the total CD8 T cell response in elite controllers is perforin-positive following HIV-specific stimulation compared to 20% in the other cohorts. However, the proportion of the HIV-specific CD8 T cell response that produces IFN-gamma does not vary widely between the groups. Elite controllers have a significantly larger proportion of responding CD8 T cells that degranulate yet remain perforin-positive following 6 hours of stimulation, suggesting that CD8 T cells in these individuals have an increased capacity to upregulate new perforin production. The cells that express perforin, which are enriched in elite controllers, display almost entirely an effector phenotype (CD27negCD45ROnegCD57+/-). Overall, there is a strong negative correlation ($p < 0.0001$) between HIV-specific perforin expression and viral load. This finding is not simply the result of the low viral load in elite controllers as HIV-specific perforin expression is not restored in HAART-suppressed patients (n = 12).

Conclusion

The rapid perforin upregulation displayed by CD8 T cells in elite controllers may contribute to the superior control of HIV replication in these subjects. Continuous perforin expression following initial antigen encounter allows for the sustained cytotoxic potential of anti-viral CD8 T cells.